U.S. FOOD & DRUG ADMINISTRATION

Information Request

Our Reference: STN: 125752/2

Information Request #26

Date: December 1, 2021

To: **Michelle Olsen, Ph.D.**
ModernaTX, Inc.
Email: Michelle.Olsen@modernatx.com

From: **Joseph Kulinski, Ph.D.**
DVRPA/OVRR/CBER
Email: Joseph.Kulinski@fda.hhs.gov

Product: COVID-19 Vaccine, mRNA (SPIKEVAX)

Subject: Analytical method procedure and validation

In reviewing BLA (STN 125752/0), we have the following information request (IR) regarding the measurement of endotoxin in the Drug Product (DP) using the (b) (4) (b) (4) LAL procedure.

1. Your procedure for measuring endotoxin in DP includes a sample "preparation" step. While you provide data demonstrating the sample (b) (4) , you have not provided data to evaluate the potential endotoxin-like activity of the lipid components of your product (b) (4) (b) (4) Please provide data to address potential endotoxin-like activity of each of the lipid components.

2. A dilution series is the usual approach to overcome DP interfering factors. Please provide data from a dilution study of (b) (4) samples that includes the percent positive product control (PPC %) recovery at each dilution of DP, up to the Maximum Valid Dilution (MVD).

3. From the data generated in the preceding request, we ask that you identify a dilution for testing DP within the range of 50-200% recovery of endotoxin, (b) (4) step. Please use this information to establish the endotoxin limit and commit to establishing specifications for DP endotoxin activity levels for

samples that are (b) (4) . Please comment and provide a date by which this can be implemented for release of DP lots.

Please confirm your receipt of this request, and provide your responses as an amendment to STN 125752 at your earliest convenience but no later than December 10, 2021.

Please contact me if you have questions and include Sudhakar Agnihothram (sudhakar.agnihothram@fda.hhs.gov) and Josephine Resnick (josephine.resnick@fda.hhs.gov) on all communications.